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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/049,556	05/07/2002	David Graham Little	RICE-006	7597

7590 12/16/2008
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EXAMINER

KANTAMNENI, SHOBHA

ART UNIT	PAPER NUMBER
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1617

MAIL DATE	DELIVERY MODE
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12/16/2008

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/049,556	Applicant(s) LITTLE, DAVID GRAHAM	
	Examiner Shobha Kantamneni	Art Unit 1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 22 September 2008.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 48-53,63-66,73,74,79 and 80 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☒ Claim(s) NONE is/are allowed.
- 6) ☒ Claim(s) 48-53,63-66,73-74,79-80 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

This office action is in response to Applicant's response filed on 09/22/2008.

Claims 48-53, 63-66, 73-74, and 79-80 are pending.

Applicant's arguments have been considered, but not found persuasive. The rejection of claims 48-53, 63, 73, and 79 under 35 U.S.C. 102(a) as being anticipated by Ke et al. (US 6,352,970) is MAINTAINED. See under response to arguments.

Applicant's arguments have been considered, but not found persuasive. The rejection of claims 48-50, 52-53, 63-66, 74, and 80 under 35 U.S.C. 102(b) as being anticipated by GEDDES (WO 93/11786, PTO-1449) is MAINTAINED. See under response to arguments.

Applicant's arguments have been considered, but not found persuasive. The rejection of claims 48-52, 63-64 under 35 U.S.C. 103(a) as being unpatentable over Yates (US 5,646,134, PTO-892 of record) is MAINTAINED. See under response to arguments.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 48-53, 63, 73, and 79 are rejected under 35 U.S.C. 102(a) as being anticipated by Ke et al. (US 6,352,970, PTO-892).

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Ke et al. discloses that Zoledronate, the specific bisphosphonate of claim 73 is capable of treating bone fractures. See column 5, lines 22-29. The mode, dosage as a single dose, site, time and regiments of administration of claims 49-53 are taught at column 16, lines 13-64, column 17, lines 1-25 and lines 40-55. It is taught that the administration can be done in a regiment to the site as determined by the patients needs. The dosage of bisphosphonates is from about 0.1 to 10 mg/kg/day. See column 15, lines 28-33. The reference also discloses that administration of zoledronate can be by transdermal, intravenous or oral routes. See column 17, lines 1-7.

With respect to the recitation “a method for promoting bone growth at a fracture site”, Ke’s method will inherently promote bone growth at a fracture site, since the method steps are same as instantly claimed.

Response to Arguments

Applicant argues that “no other step, by which an active agent (other than one or more bisphosphonates) can be administered for the promotion of bone growth, falls within the scope of the present claims.” These arguments have been considered, but not found persuasive. It is pointed out that the instant method of promoting bone growth at a fracture site uses the transition phrase “comprising the step of” which does not exclude other steps such as administering other drugs along with bisphosphonates.

Applicant argues that “it is clear that Ke does not disclose or suggest the use of only bisphosphonate(s) to promote bone growth at a fracture site. In direct contrast, the drug of the present invention consists only of at least one bisphosphonate”. This argument has been considered, but not found persuasive. Ke et al discloses that bisphosphonates

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such as Zoledronate in combination with leptin or leptin mimetic are employed in treating low bone mass or bone fractures in mammal. As discussed in the previous office action, it is pointed out again that the instant method of promoting bone growth at a fracture site uses the transition phrase “comprising the step of” which does not exclude other steps such as administering other drugs along with bisphosphonates. Accordingly, Ke’s method of administering bisphosphonates will inherently promote bone growth at a fracture site, as claimed herein since Ke’s method steps are same as the instant method steps, administering the same compound in the same amount to the same or similar patient population. See *Ex parte Novitski*, 26 USPQ 2d 1389, 1391 (Bd. Pat. App. & Int. 1993). See also *Eli Lilly and Co. v. Barr Laboratories Inc.* 251 F3d. 955; 58 USPQ2d 1869-1881 (Fed. Cir. 2001) with regard to inherency as it related to the claimed invention herein.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 48-50, 52-53, 63-66, 74, and 80 are rejected under 35 U.S.C. 102(b) as being anticipated by GEDDES (WO 93/11786, PTO-1449).

Geddes et al. disclose a method of increasing bone mass in a human afflicted with osteoporosis comprising administering a bisphosphonate administration regimen. See abstract; page 20, lines 13-27. It is disclosed that the bisphosphonate is administered at

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least 1 day of every thirty day period i.e about 4 to 6 weeks after the initial dose. See page 5, lines 25-31. It is also taught that the therapeutic regimen comprising bisphosphonate is administered for at least about twelve months or until a net skeletal mass is obtained. See page 25, lines 8-15. It is taught that the treatment regimen can comprise a combination of two or more bisphosphonates. See pages 20-22. Bisphosphonates can be administered orally as a tablet containing 0.002 mgP/kg per day, in a unit-dosage form. Administration of bisphosphonates by intraperitoneal, intravenous, parenteral, transdermal routes is also disclosed. See page 25, and page 27, bottom paragraph. It is disclosed that when a human, African-American male with a history of atraumatic fractures was administered once a week with bisphosphonate, 4-amino-1-hydroxy-1,1-bisphosphonic acid, orally as a tablet containing 0.03 mgP/kg per day, demonstrated an increase in 14.5 mg/cc spinal bone mineral, and no further atraumatic fractures were observed. See page 29, EXAMPLE 2.

With respect to the recitation “a method for promoting bone growth at a fracture site”, Gedde’s method will inherently promote bone growth at a fracture site, since the method steps are same as instantly claimed.

Thus Geddes anticipates the instant claims 48-50, 52-53, 63-66, 74, and 80.

Response to Arguments

Applicant argues that “Geddes does not teach or suggest the promotion of bone growth at a fracture site. Geddes’ disclosure of the administration of a bisphosphonate to a subject with a history of atraumatic fractures is not the same as a teaching (or suggestion) of administration to a subject with a bone fracture. The patient with the

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history of atraumatic fractures disclosed by Geddes is not said to have had a current fracture which was addressed by the treatment protocol of Geddes; instead that patient was treated for osteoporosis, which is quite different from promoting bone growth at a fracture site.” These arguments have been considered, but not found persuasive because Geddes clearly discloses a method of treating a male with atraumatic fracture by administering a bisphosphonate. See page 29, wherein it is taught that the African-american male has a history of atraumatic fracture. Thus, Geddes method of administering bisphosphonates will inherently promote bone growth at a fracture site, as claimed herein since Geddes method steps are same as the instant method steps, administering the same compound in the same amount to the same or similar patient population will cause the same effect, whether or not that effect is disclosed by the prior art.

Note that even the claiming of a new use, new function or unknown property which is inherently present in the prior art does not make the claim patentable, or would not by itself carry patentable weight if the prior art teaches the same or nearly the same method steps. See *In re Best*, 562 F.2d 1252, 1254, 195 USPQ 430, 433 (CCPA 1977). See also *Eli Lilly and Co. v. Barr Laboratories Inc.* 251 F3d. 955; 58 USPQ2d 1869-1881 (Fed. Cir. 2001) with regard to inherency as it related to the claimed invention herein.

Further, it is pointed out again that the instant method of promoting bone growth at a fracture site uses the transition phrase “comprising the step of” which does not exclude

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other steps such as administering other drugs along with bisphosphonates. Thus Geddes anticipates the instant claims 48-50, 52-53, 63-66, 74, and 80.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 48-52, 63-64 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yates (US 5,646,134, PTO-892 of record).

Yates discloses a method of treating periprosthetic bone loss comprising administering bisphosphonate to a patient such as human. See column 2, lines 45-62. See column 1, lines 33-38; column 2, lines 64-67; column 4, lines 10-14; column 6, EXAMPLE. . It is also taught that localized controlled or extended release bone growth promotants are useful, since there are 5 million fractures, and 265,000 prosthetic implants per year in United States. See column 1, lines 33-39. It is disclosed that the bisphosphonate can be administered to the periprosthetic bone area systemically either orally as tablets and/or parenterally, including subcutaneous or intravenous injection, or can be delivered in a slow release form. The bisphosphonate can be administered locally to the specific periprosthetic area in need of bone growth or repair. See column 3, lines 54-66. Bisphosphonates delivered in sustained release form is useful in

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improving implant fixation for example for improving in growth of new bone into a metal prosthesis in joint reconstruction or orthopedic implants. See column 4, lines 10-13. It is also taught that the bisphosphonates can be administered by coating the orthopedic implants at the time of the implant operation. See column 4, lines 14-16. An effective dose of bisphosphonate is about 1.5 to 3000 $\mu\text{g/kg}$ per day of body weight. Effective doses for local administration are about 0.001 μg to 1 mg per application site. See column 5, lines 1-5.

Yates does not explicitly teach a method of promoting bone growth at a fracture site comprising administering to a human with a fractured bone an effective amount of bisphosphonate.

It would have been obvious to a person of ordinary skill in the art at the time of invention to administer bisphosphonate for promoting bone growth at a fracture site because 1) Yates teaches that prosthetic implants are employed to repair fractures, and 2) Yates teaches that administration of bisphosphonate improves in growth of new bone into a metal prosthesis in joint reconstruction or orthopedic implants. One of ordinary skill in the art at the time of invention would have been motivated to administer bisphosphonate to human with fractured bone with reasonable expectation of success of promoting bone growth at the fracture site, since bisphosphonates are known to be bone growth promoters.

Response to Arguments

Applicant argues that "Yates does not disclose or suggest the use of its bisphosphonate therapy at the site of a bone fracture. What is more, Yates in no way

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discloses or suggests that a bisphosphonate could be used in the absence of an implant or other device. In direct contrast, promotion of bone growth at the site of a bone fracture is required by the present claims.” These arguments have been considered, but not found persuasive. Yates need not teach that bisphosphonate could be used in the absence of an implant or other device. Yates teaches that localized controlled or extended release bone growth promotants are useful, since there are 5 million fractures, and 265,000 prosthetic implants per year in United States i.e Yates teaches that bone growth promotants are useful when prosthetic implant are employed for fixing fractures. Yates further clearly teaches that bisphosphonate can be administered to the periprosthetic area in need of bone growth or repair i.e Yates clearly teaches that bisphosphonate can be employed for promoting bone growth. See column 3, lines 54-66; column 5, lines 56-58. Yates teaches that bisphosphonates delivered in sustained release form is useful in improving implant fixation by improving in growth of new bone into a metal prosthesis in joint reconstruction or orthopedic implants. One of ordinary skill in the art at the time of invention would have been motivated to administer bisphosphonate to human with fractured bone with reasonable expectation of success of promoting bone growth at the fracture site, since bisphosphonates are known to be bone growth promoters.

Conclusion

No claims are allowed.

THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period, will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shobha Kantamneni whose telephone number is 571-272-2930. The examiner can normally be reached on Monday-Friday, between 7.30am-3.30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan, Ph.D can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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Shobha Kantamneni, Ph.D

Patent Examiner

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/SREENI PADMANABHAN/

Supervisory Patent Examiner, Art Unit 1617